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Review article

# Clinical guidelines for male lower urinary tract symptoms associated with non-neurogenic overactive bladder☆

CME Credits

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ABSTRACT

The purpose of this guideline is to direct urologists and patients regarding how to identify overactive bladder (OAB) in male patients with lower urinary tract symptoms (LUTS) and to make an accurate diagnosis and establish treatment goals to improve the patients' quality of life (QoL). LUTS are commonly divided into storage, voiding, and postmicturition symptoms, and are highly prevalent in elderly men. LUTS can result from a complex interplay of pathophysiologic features that can include bladder dysfunction and bladder outlet dysfunction such as benign prostatic obstruction (BPO) or poor relaxation of the urethral sphincter. Diagnosis of OAB in male LUTS leads to accurate diagnosis of pure OAB and bladder outlet-related OAB, and appropriate treatment in men with residual storage symptoms after treatment for LUTS.



## 1. Purpose

The purpose of this guideline is to direct urologists and patients regarding how to identify overactive bladder (OAB) from male patients with lower urinary tract symptoms (LUTS) and to make an accurate diagnosis and establish treatment goals to improve patients' quality of life (QoL).

## 2. Male LUTS and OAB – background

*2.1.* LUTS are highly prevalent among older men and have a negative impact on health-related QoL (HRQoL). (LE 1a, Grade A) OAB is associated with medical diseases such as diabetes and congestive heart failure. (LE 2b, Grade B) OAB and urinary incontinence symptom severity progress dynamically and are also sustained over time. (LE 2a, Grade B)

OAB is a clinical diagnosis defined by the International Continence Society as the presence of "urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of a urinary tract infection or other obvious pathology".[1] OAB symptoms can be bothersome and can negatively affect HRQoL, increase anxiety and depression, and increase health care usage. The strongest predictor of OAB-associated bother was urinary urgency.[2] OAB also adversely affects sexuality in both men and women.[3] OAB is common in older adults and is associated with substantial impairment in mental health and HRQoL, but rates of treatment seeking behavior are low.[4]

Urgency is the core symptom for the presence of OAB. It has been estimated that 10–16% of the population in the world has the OAB condition.[5] However, although an urgency severity scale has been suggested, the grade of urgency is reported subjectively by the patients; therefore, there could be a wide variation among different grades of the reported urgency severity.[6]

The incidence of LUTS, including OAB in men, increases with age. Frequent comorbidity with potential prostatic disease adds complexity to the management of male LUTS.[7] In addition, patients with congestive heart failure had more storage urinary symptoms suggestive of OAB than did the age-matched controls.[8] Patients with type 2 diabetes mellitus present more OAB symptoms such as urgency and nocturia than controls. Among diabetic patients, a higher glycosylated hemoglobin level represents an independent predictor of OAB/urgency, urge urinary incontinence and nocturia.[9]

OAB and urinary incontinence symptom severity progress dynamically and are also sustained over time. Although symptom

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severity progresses dynamically, for many individuals, symptoms also persist over long time periods.[10]

*2.2.* OAB is also prevalent in men and frequently associated with LUTS in men. Men with bladder outlet obstruction (BOO) may have OAB symptoms, but OAB may exist independently of BOO in elderly men. (LE 2a, Grade B) Antimuscarinics, in combination with alpha1-receptor antagonists, or alone, improve OAB symptoms in men with and without BOO. (LE 1a, Grade A)

The prevalence of moderate/severe urinary incontinence was 4.5% in men. Prevalence increased with age from 0.7% at 20–34 years old, to 16.0% at ≥ 75 years old ($p < 0.001$).[11] It has been estimated that 29.8 million adults aged ≥ 40 years in the United States have bothersome OAB symptoms. The prevalence of OAB symptoms at least "sometimes" was 27.2% in men.[12] In a longitudinal population-based survey, urinary incontinence and other LUTS constitute dynamic conditions. There was a marked overall increase in the prevalence of urinary incontinence, OAB, and nocturia in the same individual from 1991 to 2007.[13]

Recent concepts on male incontinence have shifted from benign prostatic obstruction (BPO), BOO, or post-radical prostatic surgery to the bladder conditions. Other important pathological conditions such as nocturnal enuresis and postmicturition dribbling are also clinically relevant.[14] Among the LUTS, storage LUTS was more prevalent than voiding or postmicturition LUTS in men (44.6%, 28.5%, 15.9%, respectively). The most prevalent LUTS was nocturia (36.6%) in men.[15] Men with bothersome OAB were significantly more likely to seek treatment and report the lowest levels of HRQoL.[16]

The overall incidence of detrusor overactivity (DO) was 76.1% in male OAB patients, 63% of men with urgency (OAB dry) had DO, while 93% of men with urgency and urgency urinary incontinence (OAB wet) had DO. There was a better correlation in results between OAB symptoms and the urodynamic diagnosis of DO in men than in women, more so in OAB wet than in OAB dry.[17]

Pharmacotherapies that target the prostate often fail to alleviate OAB symptoms, and may not be the most appropriate therapy for men with storage LUTS. Multiple studies have suggested that antimuscarinics alone or in combination with alpha1-receptor antagonists improve OAB symptoms in men with and without BOO. Therefore, in the diagnosis and treatment of male LUTS associated with OAB, greater understanding of the pathophysiology of OAB that underlies male LUTS, and examination of the relationship between symptoms and urodynamic findings are needed.[18]

## 3. Clinical symptoms – urgency is core symptom

*3.1.* Diagnosis of OAB in male patients with LUTS should be based on symptom of urgency with/without urgency incontinence. (Grade A) The grade of urgency should be carefully evaluated and BOO, neurogenic lesions, and cognitive function should be carefully assessed prior to making a final diagnosis of idiopathic OAB. (Grade A)

Men with LUTS commonly experience coexisting storage, voiding, and postmicturition symptoms.[15] LUTS, OAB, urinary incontinence, and LUTS/BOO are highly prevalent conditions, emphasizing the need for comprehensive urological assessments of LUTS in men.[19,20] The prevalence of incontinence ranges from 11% to 34% among community-dwelling men aged ≥ 65 years. Benign prostatic hyperplasia (BPH)-related incontinence may be related to progression of BPH or as a postsurgical complication.[21]

Urgency should be the primary or co-primary endpoint for future studies of OAB and detrusor overactivity. Greater clarity is needed in the development of instruments for measuring urgency, so that they do not confuse urgency with normal bladder sensations; more education and guidance are needed on how urgency is defined.[22] Urgency sensation scales or urgency severity scales (USS) have been developed to assess the urinary urgency in men with LUTS-associated OAB.[23] A high urgency severity score (USS) recorded in conjunction with a voiding diary and OAB wet were strongly associated with urodynamic DO.[24]

BPH patients with DO may neglect the symptom of urgency due to abnormal bladder sensation, or negate the symptom by subconscious sphincter contraction to abort the overactivity. Among the 84 BPH-DO patients, 52 reported the symptom of urgency while 32 did not.[25]

First sensation ratio and bladder urgency velocity statistically significantly correlated with the Urgency Perception Score Urodynamic variables correlated with bladder sensation questionnaire scores and may be an objective method to assess sensory dysfunction.[26] Reduced bladder sensation is defined as bladder volume at the first sensation > 300 mL. Increased bladder sensation is defined as bladder volume at the first sensation < 100 mL.[27]

## 4. Diagnostic tests and differential diagnosis of idiopathic OAB from BOO associated OAB and other bladder conditions

*4.1.* The initial assessment of OAB in men with LUTS should include the past history, present illness, physical examination, and laboratory examination. (Grade A) In men with BPH and OAB symptoms, the OAB is usually secondary to BOO. In men, BOO is not likely, and the OAB symptoms might be idiopathic. (Grade D)

Patients presented with urgency frequency symptoms which could be due to psychological factors, increased urine production, uninhibited urge due to central nervous lesions, or having DO. Urgency symptom can be caused by sensory dysfunction (hypersensitive bladder) or DO. Sensory urgency might be due to micromotion of the detrusor during bladder filling (increased excitability), rapid bladder filling or diuresis, urothelial dysfunction, or a high sensory perception due to anxiety, depression, or emotional stress. A differential diagnosis of OAB should exclude other pathologies such as psychological distress, interstitial cystitis, UTI, bladder tumor, and urolithiasis.

### *4.1.1. Past history*

A family history of prostatic disease and prostatic cancer, previous history of lower urinary tract diseases such as bladder stone, cystoscopic examination, transurethral surgery, any systemic disease (diabetes, hypertension, cerebral vascular accident, Parkinson's disease (PD), chronic obstructive pulmonary disease, asthma, etc.), and medical history (alpha-blocker, 5-alpha-reductase inhibitor, antimuscarinics, neurological medication) should be recorded.

### *4.1.2. Present illness*

The duration of LUTS (acute or chronic onset) and associated symptoms should be recorded. The LUTS can be assessed using the International Prostate Symptom Score (IPSS) or the American Urological Association Symptom Index (AUA-SI).[28] The total symptom score can be classified as mild (< 8), moderate (8–19), and severe (> 20).[29] The dominant symptoms should be assessed according to the storage and empty symptoms, separately. Daily fluid intake is important. Excessive fluid intake can produce voiding patterns that mimic OAB symptoms. A fluid diary can be helpful in

this regard. In community-dwelling healthy adults, normal frequency consists of voiding every 3–4 hours, with a median of approximately six voids/day.[30] Comorbid conditions such as neurologic diseases and other genitourinary conditions should be considered as they directly impact bladder function. In addition, polydipsia and polyuria-related frequency might be considered in differential diagnosis; a frequency volume chart is helpful.

#### 4.1.3. Physical examination

Patients should be examined systemically and locally. The presence of an abdominal scar, a palpable distended bladder, and genital lesion should be carefully examined. Digital rectal examination (DRE) for the prostatic consistency, prostatic size, surface, and any abnormal nodularity should be carefully examined. In addition, a focal neurological examination such as bulbocavernosus reflex, anal sphincter contraction, and saddle sensation should be examined during DRE.

#### 4.1.4. Laboratory tests

When a patient complains of urethral symptoms (micturition pain, burning sensation), a urinalysis should be performed. When the urinalysis shows microscopic hematuria or pyuria, a kidney ureter bladder (KUB) X-ray should be ordered to investigate the presence of a bladder or lower ureteral stone. Blood urea-nitrogen and creatinine levels should be investigated when chronic urinary retention is noted. Prostatic specific antigen (PSA) level is indicated in all patients with an enlarged prostate or abnormal DRE finding, except in the elderly (e.g., > 80 years old).

#### 4.1.5. Urodynamic study

Uroflowmetry (including maximum flow rate, voided volume, and flow pattern) and subsequent postvoid residual (PVR) should be measured concomitantly. Bladder sonography is indicated to measure the PVR and to investigate bladder stone, bladder wall thickness,[31] and intravesical prostatic protrusion.[32] Increased bladder wall thickness and intravesical prostatic protrusion have been demonstrated to be associated with BOO and OAB symptoms. Mean bladder wall thickness is associated with a symptom history of OAB and mixed urinary incontinence (MUI), higher daytime and night time frequency, and higher visual analog scale (VAS) scores.[31]

Although a uroflow study has been found to have poor diagnostic specificity for BOO,[29] uroflowmetry should be performed in men with LUTS and OAB. A cystometry or pressure flow study is not recommended as the first line investigation for OAB diagnosis unless the initial treatment fails based on the clinical symptoms and uroflowmetry.

#### 4.1.6. OAB questionnaires

OAB, especially in patients with urgency incontinence, eventually has a negative impact on HRQoL. Urinary frequency can be reliably measured with a voiding diary. Traditionally, up to seven micturition episodes during waking hours has been considered normal.[33] However, because multiple factors might cause confusion of OAB, multi-item questionnaires have been introduced to evaluate the impact of OAB and of treatment outcomes, such as OAB symptom score (OABSS) and OAB-q.[16,34,35] By contrast, there is no disease-specific HRQoL instrument that serves as a “gold standard” for OAB patients.[36]

Kelleher et al[37] published the King's Health Questionnaire (KHQ) which covered dimensions of importance to OAB patients, particularly urgency and frequency. The KHQ was developed with patient input and has been validated in a large cohort of incontinent women. The bladder problem question of the KHQ shows the greatest promise as single-item scales to assess problem intensity in OAB patients.[38] This questionnaire is also validated in Chinese and was demonstrated to be a reliable instrument for the assessment of HRQoL in patients with OAB.[39]

Measuring IPSS subscores and calculating IPSS-V/S is a simple and useful method to differentiate failure to voiding and failure to storage LUTD in men with LUTS. IPSS-V/S may provide a guide for the initial treatment, especially for primary care physicians without access to urological studies.[40] Initial treatment with doxazosin for patients with IPSS-V/S > 1 and tolterodine for patients with IPSS-V/S $\leq$ 1 is safe and feasible.[41] Combination of IPSS-T with total prostate volume (TPV) and Qmax increases the PPV of bladder outlet-related LUTD. Furthermore, including IPSS-V/S > 1 or > 2 into the equation results in a higher PPV than IPSS-T. IPSS-V/S > 1 is a stronger predictor of bladder outlet-related LUTD than IPSS-T.[42]

## 5. Differential diagnosis between idiopathic OAB and neurogenic OAB

*5.1.* Although this guideline does not deal with neurogenic voiding dysfunction, elderly men with LUTS and OAB might also have latent neurological lesions that may not be discovered at the initial examination. (LE 2a, Grade B) A detailed history taking and neurological examination including bulbocavernosus reflex, deep tendon reflex test, and saddle anesthesia will be helpful in differentiation between idiopathic and neurogenic OAB. (Grade A)

LUTS are highly prevalent in stroke patients and have a major impact on daily life. The most frequent symptom was nocturia (76%) followed by urgency (70%), and daytime frequency (59%). The most severe symptom was urgency followed by nocturia, and daytime frequency.[43] Double incontinence (urinary and fecal incontinence) was more prevalent than isolated incontinence in patients after stroke during post-acute rehabilitation.[44]

In patients with stroke and voiding dysfunctions, a careful urodynamic study should be performed to identify the presence of BOO or dysfunctional voiding. Voiding dysfunction is also a significant problem in patients with a head injury. Bladder hyperreflexia is seen in patients with injuries above the pontine micturition center. The voiding abnormality has a good prognosis and resolves spontaneously.[45]

The most prevailing urinary symptom in idiopathic PD (IPD) was nocturia (77.5%) followed by urgency (36.7%), and frequency (32.6%). Urodynamic tests revealed neurogenic DO in 33 patients (67.3%), detrusor underactivity in six patients (12.2%), and 10 (20.4%) patients with normal detrusor function. The irritative urinary symptoms manifested urodynamically as neurogenic detrusor overactivity are more common in IPD patients than obstructive symptoms.[46]

One study investigated the LUTS and urodynamic and cystometric findings in PD, dementia with Lewy bodies, and Alzheimer's disease (AD). Urgency and urge incontinence are more prevalent in dementia with Lewy bodies than in PD and AD, whereas mean voided volume, free flow, cystometric bladder capacity, and detrusor pressure were similar in the groups; DO in 92% of the patients with dementia with Lewy bodies, 46% of the patients with PD, and 40% of the patients with AD.[47]

In the dedicated diabetic center in which all patients were screened, 22.5% had OAB, and 48.0% of those with OAB had incontinence.[48] After multivariate analysis, age and male sex, and age and waist circumference were independent risk factors for OAB and OAB wet, respectively, however, glycated hemoglobin and C-reactive protein levels were not. This finding suggests that the severity of diabetes mellitus (DM) contributes little to OAB. Men with DM and LUTS can present with varied urodynamic findings, apart from the classic sensory or motor cystopathy. Urodynamic studies showed impaired first sensation (> 250 mL), increased capacity

(> 600 mL), detrusor underactivity, DO, high PVR urine volume (more than one third of capacity), and BOO (Abrams-Griffiths number > 40) in 23.1%, 25.0%, 78.8%, 38.5%, 65.4%, and 28.8% of the men, respectively.[49]

Men with DM and LUTS can present with DO, detrusor underactivity, and BOO. Noninvasive tests did not allow the identification of these. Only urodynamic evaluation is able to determine symptom etiology. There is a relatively low prevalence of BOO in diabetic patients with prostate enlargement and LUTS. Of the 50 patients in the study, 23 (46%) had BOO. There was no correlation between the IPSS, uroflowmetry, PVR urine or prostate volume, and the presence of BOO ($p > 0.05$). Noninvasive tests did not allow the identification of these. Only urodynamic evaluation is able to determine symptom etiology.[50]

## 6. Urodynamic study for OAB in male LUTS

*6.1.* Male LUTS may originate from bladder dysfunction or bladder outlet disorders. (LE 2b, Grade B) DO and urethral sphincter dysfunction should also be considered in young men with LUTS or small prostate. (LE 2b, Grade B)

LUTS in men is highly prevalent and storage LUTS is more prevalent than voiding or postmicturition symptoms.[7,11,51] Although OAB wet is usually associated with urodynamic DO, the OAB symptoms might involve other bladder dysfunction or outlet disorders. Initial treatment based on predominant symptoms without urodynamic testing is encouraging, but a urodynamic test is recommended when the initial management fails to resolve the storage LUTS.

A urodynamic study is useful in the evaluation of young men presenting with LUTS; abnormal urodynamic findings were noted in 36 (72%) patients, including DO in nine (18%) patients, detrusor underactivity/acontractility in five (10%) patients, and BOO in 21 (42%) patients. Fourteen (28%) individuals had primary bladder neck dysfunction and five (10%) individuals had BPH.[52] About one third of men with LUTS who were > 55 years of age had BPO. Patients < 55 years old were more likely to have poor relaxation of the urethral sphincter as a likely cause of LUTS.[53] In a group of men with LUTS and small prostate, BOO was the main finding, affecting 50.0% of the patients, followed by detrusor underactivity (DU) in 41 (48.8%) patients and DO in 28 (33.3%) patients.[54]

*6.2.* Urodynamic testing is indicated especially when male patients with LUTS are ready to undergo invasive therapy for LUTS, such as transurethral resection of the prostate (TURP) or laser prostatectomy. (LE 2b, Grade B) More clinically objective parameters should be investigated to provide a high correlation with urodynamic results such as BOO or DO, to achieve a higher success rate of treatment outcome of LUTS in men. (Grade D)

Because the correlation between LUTS, DRE, cystoscopy with BOO is poor,[55] a urodynamic study has been regarded as the only way of establishing the diagnosis of BOO.[56] Although a urodynamic study is not necessary in the short term treatment of LUTS/BPH, most urologists believe that a pressure flow study should be undertaken before surgery in neurologically normal men with LUTS and a low Qmax,[57] and men with LUTS and voiding dysfunction of uncertain etiology.

There were weak correlations between OAB symptoms and urodynamic findings. Most men with OAB symptoms had concomitant voiding symptoms and more than one third (43%) of these had evidence of BOO.[58] A pressure flow study provides valuable information on detrusor function, however, a urodynamic study also has some morbidity, such as urinary tract infection in 4–6%, and dysuria in 75% of men with BOO and 55% of men without BOO.[59] Although a pressure flow study can establish the diagnosis of BOO, the symptomatic outcome of treatment modalities for BPH did not differ among different degrees of BOO.[60]

A videourodynamic study provides a more accurate diagnosis of BPO and other bladder and urethral conditions responsible for LUTS, such as DO, impaired detrusor contractility, hypersensitive bladder, poor relaxation of urethral sphincter, bladder neck dysfunction, pseudodyssynergia, detrusor underactivity, and normal bladder and urethra.[61] In patients with both storage and empty LUTS, the incidence of DO increases with age, while the incidence of poor relaxation of urethral sphincter increases as age decreases.[53]

In patients with clinical BPH, DO is independently associated with age and BOO. Among 1418 men investigated (median age: 63 years), 864 (60.9%) had DO. In a univariate analysis, men with DO were significantly older, more obstructed, had larger prostates, higher irritative IPSS subscores, a lower voiding volume at free uroflowmetry, and a lower bladder capacity at cystometry.[62]

OAB is a symptom syndrome which includes either sensory dysfunction or a combination of sensory and motor disorders of the urinary bladder. In a group of men and women with persistent storage symptoms, 89% of patients whose primary symptoms were frequency and urgency had urodynamic DO.[63] Not all patients with OAB can have uninhibited detrusor contractions occurring during bladder filling. A urodynamic study can only detect about 50% of patients with OAB symptoms.[64] BOO may cause DO, however, many studies have reported only 45–50% of men with LUTS have urodynamically confirmed DO and BOO.[65,66]

The ageing process results in intrinsic urethral sphincteric deficiency which increases the prevalence of urinary incontinence and may potentiate DO and OAB symptoms. Under this consideration, a urodynamic study has been considered as useless in the diagnosis of OAB. However, a urodynamic study is essential in differential diagnosis of etiologies of OAB such as BOO, DO with impaired detrusor contractility, dysfunctional voiding, and mixed urinary incontinence.[67]

OAB symptoms of urge incontinence are found to be strongly correlated with DO in men. Hyman et al[68] found that a higher incidence of DO was associated with urge incontinence than with other LUTS in men. Of the men with LUTS, 68% had BOO, including 46% of men with DO. Hashim and Abrams[69] found that the correlation between OAB symptoms and urodynamic DO was better in men than in women. Sixty-nine percent of men and 44% of women with urgency (OAB dry) had DO, while 90% of men and 58% of women with urgency and urgency incontinence (OAB wet) had DO. They concluded that the bladder is a better and more reliable witness in men than in women. The incidence of urodynamic DO was more commonly seen in patients with BOO such as BPH, bladder neck dysfunction, and DSD, but not in those with bladder sensory disorder and an underactive bladder. A urodynamic study is necessary if clinical presentations favor pathological causes other than hypersensitive bladder.[53]

In the clinical practice, treatment of OAB is based on the subjective symptoms of urgency and frequency; treatment with antimuscarinics in patients without DO might fail. A significant increase in bladder capacity during the cystometric study was shown only in patients with DO, whereas no statistically significant improvement was shown in patients without DO. Treatment with solifenacin was shown to be effective only in patients with involuntary detrusor contractions at the cystometric study.[70] However, one study revealed that urodynamics status could not predict treatment outcomes between patients treated with tolterodine-extended released (ER) or placebo, suggesting that anticholinergic

treatment may be initiated in patients with OAB symptoms without the need for urodynamics studies.[71]

A recent study assessed the effects of onabotulinumtoxinA (Botox) on clinical and urodynamic variables in patients with idiopathic OAB. Improvements in urodynamic parameters and clinical outcomes generally trended together following onabotulinumtoxinA treatment, with or without baseline DO. Therefore, successful idiopathic OAB treatment with onabotulinumtoxinA does not appear to be related to the pretreatment finding of DO.[72]

## 7. Conservative treatment – behavioral modification, percutaneous tibial nerve stimulation, and sacral nerve stimulation

*7.1.* Patients should be educated about drinking habits and lifestyle modification as the first line treatment of OAB before medication is started. (LE 2b, Grade B) Most OAB treatments improve patient symptoms but are unlikely to eliminate all symptoms. (LE 1b, Grade B) Patients should be encouraged to continue behavioral modification even though they are successfully treated with medication. (LE 2b, Grade B)

Initial management of OAB-associated male LUTS included basic diagnostic tests to exclude an underlying disease or condition such as UTI. Treatment is mostly conservative (lifestyle interventions, physiotherapy, physical therapy, pharmacotherapy) and is of an empirical nature.[73]

Behavioral therapy and pelvic floor muscle training have been tried to relieve this bothersome syndrome. Behavioral therapy for OAB includes regular water intake (1.5–2 L daily), time voiding, inhibiting urge sensation, and avoiding irritants or diuretics. These behavioral modifications should be conducted after excluding BOO, contracted bladder, or other bladder pathologies.[74] The aim of bladder re-education is to teach the central nervous system (CNS) memory to accommodate bladder sensation and elevate the sensory threshold of voiding desire.

Most OAB patients do not experience complete symptom relief; most patients experience significant reductions in symptoms and improvements in QoL. Behavioral therapy with bladder drill provides effective therapy results for OAB.[75,76] Weight loss also has positive effects on older women with incontinence.[77] Fluid management with a 25% reduction in fluid intake reduced frequency and urgency.[78] A bladder training study reducing caffeine intake also resulted in reductions in voiding frequency.[79] Behavioral treatments are generally either equivalent to or superior to medications in terms of reducing incontinence episodes, improving frequency, and improving QoL.[80–82]

## 8. Medical treatment – for BOO, alpha-blocker, antimuscarinics, and combined therapy

*8.1.* Antimuscarinics or beta-3 adrenoceptor agonists are recommended for men with LUTS suggestive of OAB and without evidence of BOO. (LE 1a, Grade A) Men with both voiding and storage LUTS are recommended to take alpha-blockers with/without 5-alpha-reductase inhibitors (5ARI) first, followed by antimuscarinics (LE 2a, Grade B) or beta-3 adrenoceptor agonists. (Grade D)

Traditional medication for OAB is antimuscarinic agents targeting the muscarinic receptors. Through blockage of receptors, the contractility of the detrusor smooth muscle decreases and the symptoms of OAB can be relieved. The role of muscarinic M2 receptors is found to inhibit the relaxation effect of norepinephrine mediated by the beta-3-adrenergic receptors.[83] In this regard, an antimuscarinic agent that has both M2 and M3 antagonist effects may directly inhibit detrusor contraction and indirectly inhibit the inhibitory effect of detrusor relaxation, and therefore have a better therapeutic effect on OAB compared to that having a selective M3 antimuscarinic effect. Clinicians should offer oral antimuscarinics, including darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, or trospium as first line antimuscarinic therapy. However, not all patients can benefit from an antimuscarinic agent. Some patients with OAB and hypersensitive bladder may respond to antimuscarinic agents.[74] Adverse effects such as dizziness, dry mouth, blurred vision, and constipation might be intolerable for some elderly patients.[84]

Treatment for LUTS suggestive of BPH has traditionally involved the use of alpha-1 adrenoceptor antagonists, 5ARI, and phytotherapy. This treatment can effectively improve OAB symptoms in most patients with BOO and OAB. The focus of treatment for LUTS has thus shifted from the prostate to the bladder and other extraprostatic sites.[85] Selective beta-3 adrenoceptor agonists and antimuscarinics are potentially useful agents for treating LUTS, particularly for storage symptoms secondary to outflow obstruction. Oral antimuscarinics are usually used as second line therapy for male LUTS-associated OAB, reducing symptoms, but are commonly associated with non-life-threatening side effects (e.g., dry mouth, constipation, dry eyes, blurred vision, dyspepsia, UTI, urinary retention, impaired cognitive function). There is no compelling evidence for differential efficacy across medications.

Combination treatment with an alpha-blocker (tamsulosin) plus an anticholinergic (tolterodine) improves QoL in patients with BOO and concomitant detrusor instability. Interestingly, no acute urinary retention was observed and tolterodine did not affect the quality of urine flow or residual urine volume.[86] The efficacy of antimuscarinics has been proven in different trials regarding different storage symptom end points only in men with low PVR urine volumes at baseline (< 200 mL). Overall, the addition of an antimuscarinic to the treatment of a patient with BOO and concomitant OAB seems to offer an amelioration of the symptoms and a moderate improvement in QoL.[87] However, first line antimuscarinic monotherapy has been proven safe and effective within 12 weeks in selected patients with BPH. Higher baseline IPSS-S, higher baseline Qmax, and lower TPV were predictors of successful antimuscarinic monotherapy.[88]

OAB is an abnormal bladder condition; sensory receptors or beta-adrenergic receptors might overexpress and cause abnormal clinical presentation. For patients whose OAB symptoms were refractory to an antimuscarinic agent, a newly launched beta-3 adrenergic agonist might be therapeutically effective. Solabegron significantly reduced the symptoms of OAB in women with moderate to severe OAB. Solabegron was safe, well tolerated, and did not demonstrate significant differences in adverse events (AEs) as compared to placebo. Beta-3 adrenoceptor agonists may represent a new therapeutic approach for treating OAB symptoms.[89]

*8.2.* In patients with OAB refractory to the first line treatment, adding a second antimuscarinic is feasible. (LE 2b, Grade B) However, the adverse effects should be balanced for long term treatment. (LE 3b, Grade B)

Clinicians should not use antimuscarinics in patients with narrow angle glaucoma unless approved by the treating ophthalmologist and should use antimuscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention. If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one antimuscarinic

medication, then a dose modification or a different antimuscarinic medication may be tried. Clinicians should manage constipation and dry mouth before abandoning effective antimuscarinic therapy. Management may include bowel management, fluid management, dose modification, or alternative antimuscarinics. Clinicians must use caution in prescribing antimuscarinics in patients who are using other medications with anticholinergic properties. Clinicians should use caution in prescribing antimuscarinics in frail elderly patients, particularly the elderly; the potential CNS adverse effects of each anticholinergic agent must be weighed against the severity of OAB symptoms.[90] Nevertheless, in older men with BPH and storage symptoms treated with alpha-blockers and/or 5ARI, additive treatment with tolterodine ER in older men with BPH/BOO and significant storage symptoms has been proven to be a beneficial and safe therapeutic option.[91] Several recent trials also proved that adding antimuscarinics to an alpha-blocker provided individuals with improvement of residual OAB symptoms in men with LUTS.[51,92–94]

## 9. Minimally invasive therapies for OAB

*9.1.* Botulinum toxin A 100 U is recommended in patients with refractory OAB, excluding patients with BOO. (LE 1a, Grade A) Ageing patients with medical comorbidity or a PVR > 100 mL should be carefully informed of the risks of urinary retention or UTI. (LE 2a, Grade B)

Intravesical injection of onabotulinumtoxinA is effective for idiopathic DO refractory to antimuscarinics. Several randomized, placebo-controlled studies have proven that onabotulinumtoxinA 100 U was well tolerated and produced significantly and clinically relevant improvements in all OAB symptoms, patient-reported benefits, and HRQoL in patients inadequately managed by anticholinergics.[95–97] Improvement of urgency severity is significantly associated with a higher success rate at 3 months and a longer therapeutic duration after intravesical botulinum toxin-A (BoNT-A) injection for idiopathic detressor overactivity (IDO).[98] However, safety is a major concern, especially in elderly individuals. Although safety and efficacy were similar between elderly patients without frailty and younger patients, an increased risk of large PVR urine volume and a lower long term success rate in frail elderly patients were noted after intravesical onabotulinumtoxinA injection for refractory idiopathic detrusor overactivity.[99]

A single onabotulinumtoxinA treatment, with doses $\geq$ 100 U, resulted in statistically significant and clinically meaningful improvement in HRQoL by Week 2 compared with placebo, and this improvement was sustained for $\leq$ 36 weeks in patients with idiopathic OAB and urgency urinary incontinence who were inadequately managed by oral antimuscarinics.[97] A total of 207 injections were performed in 100 patients. BoNT-A can provide a safe and effective medium term management option for patients with refractory IDO. The most common reasons cited for stopping treatment were poor efficacy and clean intermittent self catheterization (CISC)-related issues.[100] Intravesical injection of BoNT-A provides effective treatment for DO and OAB. However, the high rates of treatment-related AEs prevent its more widespread use. Male sex, baseline PVR $\geq$ 100 mL, comorbidity, and BoNT-A dose > 100 U are risk factors for an increasing incidence of AEs after intravesical BoNT-A injection for IDO.[101]

Intravesical BoNT-A therapy is an effective short term treatment for OAB. With time, two-thirds of patients (61.3%) had discontinued intravesical BoNT-A therapy at 36 months, with a 63.8% discontinuation rate at 60 months. The main reasons for discontinuation were tolerability issues, mainly urinary tract infections and the need for clean intermittent self-catheterization. Primary and secondary losses of efficacy were of secondary importance.[96]

*9.2.* Percutaneous tibial nerve stimulation and sacral nerve stimulation may be considered as a clinically significant alternative therapy for OAB. (LE 3b, Grade B)

Electrostimulation is an established therapeutic option for neurogenic urinary disorders. Chronic transcutaneous posterior tibial nerve stimulation was also shown to be effective in the management of severe OAB, without compromising bladder emptying or inducing side effects. Treatment may be effective even in the absence of an acute cystometric effect.[102] A randomized, multicenter, controlled study compared the effectiveness of percutaneous tibial nerve stimulation to extended-release tolterodine. The reduction in OAB symptoms along with global response assessments were evaluated. The study demonstrates that percutaneous tibial nerve stimulation is safe with statistically significant improvements in patient assessment of OAB symptoms, and with objective effectiveness comparable to that of pharmacotherapy. Percutaneous tibial nerve stimulation may be considered a clinically significant alternative therapy for OAB.[103] After 12 weeks, individuals randomized to weekly percutaneous tibial nerve stimulation were offered an additional 9 months of treatment with assessments at 6 months and 12 months from baseline. The durability of response demonstrates the effectiveness of percutaneous tibial nerve stimulation as a viable, long term therapy for OAB.[104] Posterior tibial nerve stimulation can benefit a carefully selected group of patients with moderately severe baseline incontinence and frequency and willingness to comply with the posterior tibial nerve stimulation protocol.

Sacral nerve stimulation (SNS) is thought to act via stimulation of somatic afferents which inhibit the transmission of afferent messages arising from the bladder.[105] Therefore, SNS has been applied to improve urgency, frequency, and urge incontinence.[106] A retrospective review performed on SNS patients who received an implantable pulse generator, from December 1993 to December 2004, demonstrated that SNS is an effective method for treating certain types of voiding dysfunction. Although 53% of patients experienced at least one RE, 97% of patients were mild to moderate and did not appear to affect the continued use of this therapy.[107] The carryover effect could be caused by negative modulation of excitatory synapses in the central micturition reflex pathway.[108]

Although the mechanisms of neuromodulation remain unclear, this therapeutic modality has been used to treat patients with OAB and who are refractory to conventional therapies. However, patients should be informed about the frequent and moderately severe AEs, including pain at the stimulator and lead sites, lead migration, infection/irritation, electric shock, the need for additional surgeries (a side effect that occurred in > 30% of patients), and periodic battery replacement.

## 10. Surgical treatment

*10.1.* Although most patients with OAB can be successfully treated with oral medication and intravesical treatments, some patients might still be refractory to treatment. For those patients suffering from intractable OAB symptoms, we should search for the possible uncovered pathologies including residual BOO, urethral incompetence, and contracted bladder and perform the appropriate surgery. (LE 3b, Grade B)

OAB associated with male LUTS/BPH can be relieved after surgical prostatectomy. TURP significantly reduces the incidence of detrusor overactivity concurrent with BOO.[109] A multivariate

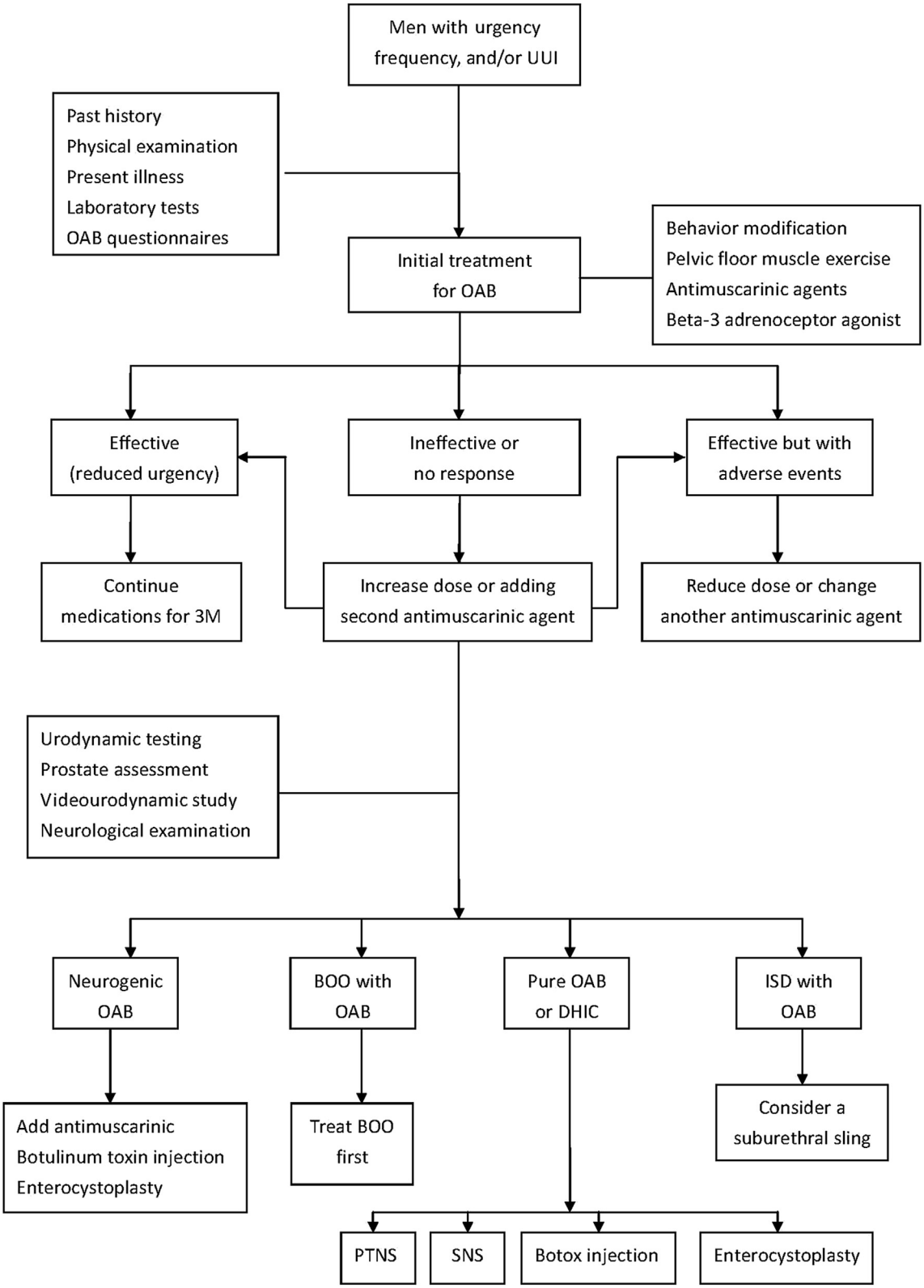


**Fig. 1.** The algorithm of diagnosis and treatment of male overactive bladder syndrome. BOO = bladder outlet obstruction; Botox = botulinum toxin; DHIC = detrusor hyperactivity and inadequate contractility; ISD = intrinsic sphincter deficiency; OAB = overactive bladder syndrome; PTNS = posterior tibial nerve stimulation; SNS = sacral nerve stimulation; UUI = urgency urinary incontinence.

analysis suggested that the baseline degree of detrusor contractility was consistently associated with the improvement in each OAB symptom and good detrusor contractility is essential for the symptomatic benefits after the surgical relief of BOO. Aging males with good urinary flow rates appear to experience a reduced improvement of nocturia symptoms after undergoing TURP.[110]

Enterocystoplasty is more helpful in intractable DO than in interstitial cystitis. Detrusor myomectomy (autoaugmentation) has yielded excellent results in patients with neurogenic causes of DO. Urinary diversion is rarely required in DO, but may be preferable to enterocystoplasty when severe pelvic pain is present. Cystourethrectomy with urinary diversion or bladder augmentation is the ultimate option for the treatment of refractory DO, particularly in patients with intractable pain.[111]

When patients are refractory to nonsurgical therapies and are found to have a contracted bladder or low bladder compliance, enterocystoplasty using a segment of terminal ileum or the ileocecal portion is feasible to rebuild a low pressure, large compliant bladder that may resolve the OAB symptoms within 3 months.[112] Lotenfoe et al[113] achieved an overall success rate of 73% with cystourethrectomy and colonic urinary diversion. They noted the success rate was 88% in patients with bladder capacities < 400 mL, but only 20% in patients with capacities > 400 mL.

## 11. Conclusion

LUTS are commonly divided into storage, voiding, and postmicturition symptoms, and are highly prevalent in elderly men. LUTS can result from a complex interplay of pathophysiologic features that can include bladder dysfunction and bladder outlet dysfunction such as BPO or poor relaxation of the urethral sphincter. Diagnosis of OAB in male LUTS leads to accurate treatment in men with residual storage symptoms after treatment for LUTS. An algorithm of the diagnosis and treatment of male OAB has been constructed for clinical reference (Fig. 1).

## 12. Level of evidence and grade of recommendations

| | Statement | LE | Grade |
|---|---|---|---|
| 1 | LUTS are highly prevalent among older men and have a negative impact on health-related QoL. | 1a | A |
| 2 | Antimuscarinics in combination with alpha-1 receptor antagonists, or alone, improve OAB symptoms in men with and without BOO. | 1a | A |
| 3 | Diagnosis of OAB in male patients with LUTS should be based on symptom of urgency with/without urgency incontinence. | | A |
| 4 | The initial assessment of OAB in men with LUTS should include the past history, present illness, physical examination, and laboratory examination. | | A |
| 5 | A detailed history taking and neurological examination including bulbocavernosus reflex, deep tendon reflex test, and saddle anesthesia will be helpful in differentiation between idiopathic and neurogenic OAB. | | A |
| 6 | DO and urethral sphincter dysfunction should also be considered in young men with LUTS or a small prostate. | 2b | B |
| 7 | Urodynamic testing is indicated especially when male patients with LUTS are ready to undergo invasive therapy for LUTS, such as TURP or laser prostatectomy. | 2b | B |
| 8 | Patients should be encouraged to continue behavioral modification even though they are successfully treated with medication. | 2b | B |
| 9 | Antimuscarinics or beta-3 adrenoceptor agonists are recommended for men with LUTS suggestive of OAB and without evidence of BOO. | 1a | A |
| 10 | Men with both voiding and storage LUTS are recommended to take an alpha-blocker with/without 5ARI first, followed by antimuscarinics or a beta-3 adrenoceptor agonist. | 2a | B |
| 11 | In patients with OAB refractory to the first line treatment, adding a second antimuscarinic is feasible. However, the adverse effects should be balanced for long-term treatment. | 2b | B |
| 12 | Botulinum toxin A 100 U is recommended in patients with refractory OAB, excluding patients with BOO. | 1a | A |
| 13 | For those patients suffering from intractable OAB symptoms, we should search for the possible uncovered pathologies including residual BOO, urethral incompetence, and contracted bladder, and perform appropriate surgery. | 3b | B |

## Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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## References

1. Haylen BT, Freeman RM, Swift SE, Cosson M, Davila GW, Deprest J, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint terminology and classification of the complications related directly to the insertion of prostheses (meshes, implants, tapes) and grafts in female pelvic floor surgery. *Neurourol Urodyn* 2011;**308**:2–12.
2. Milsom I, Kaplan SA, Coyne KS, Sexton CC, Kopp ZS. Effect of bothersome overactive bladder symptoms on health-related quality of life, anxiety, depression, and treatment seeking in the United States: results from EpiLUTS. *Urology* 2012;**80**:90–6.
3. Coyne KS, Sexton CC, Thompson C, Kopp ZS, Milsom I, Kaplan SA. The impact of OAB on sexual health in men and women: results from EpiLUTS. *J Sex Med* 2011;**8**:1603–15.
4. Sexton CC, Coyne KS, Thompson C, Bavendam T, Chen CI, Markland A. Prevalence and effect on health-related quality of life of overactive bladder in older Americans: results from the epidemiology of lower urinary tract symptoms study. *J Am Geriatr Soc* 2011;**59**:1465–70.
5. Milson I, Abrams P, Cardozo L, Roberts RG, Thüroff J, Wein AJ. How widespread are the symptoms of an overactive bladder and how are they managed? A population based prevalence study. *BJU Int* 2001;**87**:760–6.
6. Nixon A, Colman S, Sabounjian L, Sandage B, Schwiderski UE, Staskin DR, et al. Validated patient reported measure of urinary urgency severity in overactive bladder for use in clinical trials. *J Urol* 2005;**174**:604–7.
7. Kondo A, Saito M, Yamada T, Kato T, Hasegawa S, Kato K. Prevalence of handwashing urinary incontinence in healthy subjects in relation to stress and urge incontinence. *Neurourol Urodyn* 1992;**11**:519–23.
8. Chiu AF, Liao CH, Wang CC, Wang JH, Tsai CH, Kuo HC. High classification of chronic heart failure increases risk of overactive bladder syndrome and lower urinary tract symptoms. *Urology* 2012;**79**:260–5.
9. Chiu AF, Huang MH, Wang CC, Kuo HC. Higher glycosylated hemoglobin levels increase the risk of overactive bladder syndrome in patients with type 2 diabetes mellitus. *Int J Urol* 2012;**19**:995–1001.
10. Irwin DE, Milsom I, Chancellor MB, Kopp Z, Guan Z. Dynamic progression of overactive bladder and urinary incontinence symptoms: a systematic review. *Eur Urol* 2010;**58**:532–43.
11. Markland AD, Goode PS, Redden DT, Borrud LG, Burgio KL. Prevalence of urinary incontinence in men: results from the national health and nutrition examination survey. *J Urol* 2010;**184**:1022–7.
12. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the United States stratified by sex and age. *Urology* 2011;**77**:1081–7.
13. Wennberg AL, Molander U, Fall M, Edlund C, Peeker R, Milsom I. A longitudinal population-based survey of urinary incontinence, overactive bladder, and other lower urinary tract symptoms in women. *Eur Urol* 2009;**55**:783–91.
14. Coyne KS, Sexton CC, Kopp ZS, Ebel-Bitoun C, Milsom I, Chapple C. The impact of overactive bladder on mental health, work productivity and health-related quality of life in the UK and Sweden: results from EpiLUTS. *BJU Int* 2011;**108**:1459–71.
15. Lee YS, Lee KS, Jung JH, Han DH, Oh SJ, Seo JT, et al. Prevalence of overactive bladder, urinary incontinence, and lower urinary tract symptoms: results of Korean EPIC study. *World J Urol* 2011;**29**:185–90.

16. Coyne K, Revicki D, Hunt T, Corey R, Stewart W, Bentkover J, et al. Psychometric validation of an overactive bladder symptom and health-related quality of life questionnaire: the OAB-q. *Qual Life Res* 2002;**11**:563–74.
17. Al-Ghazo MA, Ghalayini IF, Al-Azab R, Hani OB, Matani YS, Haddad Y. Urodynamic detrusor overactivity in patients with overactive bladder symptoms. *Int Neurourol J* 2011;**15**:48–54.
18. Chapple CR, Roehrborn CG. A shifted paradigm for the further understanding, evaluation, and treatment of lower urinary tract symptoms in men: focus on the bladder. *Eur Urol* 2006;**49**:651–8.
19. Irwin DE, Milsom I, Kopp Z, Abrams P, Artibani W, Herschorn S. Prevalence, severity, and symptom bother of lower urinary tract symptoms among men in the EPIC study: impact of overactive bladder. *Eur Urol* 2009;**56**:14–20.
20. Irwin DE, Kopp ZS, Agatep B, Milsom I, Abrams P. Worldwide prevalence estimates of lower urinary tract symptoms, overactive bladder, urinary incontinence and bladder outlet obstruction. *BJU Int* 2011;**108**:1132–8.
21. Han E, Black LK, Lavelle JP. Incontinence related to management of benign prostatic hypertrophy. *Am J Geriatr Pharmacother* 2007;**5**:324–34.
22. Abrams P, Chapple CR, Jünemann KP, Sharpe S. Urinary urgency: a review of its assessment as the key symptom of the overactive bladder syndrome. *World J Urol* 2012;**30**:385–92.
23. Coyne KS, Margolis MK, Hsieh R, Vats V, Chapple CR. Validation of the urinary sensation scale (USS). *Neurourol Urodyn* 2011;**30**:360–5.
24. Chung SD, Liao CH, Chen YC, Kuo HC. Urgency severity scale could predict urodynamic detrusor overactivity in patients with overactive bladder syndrome. *Neurourol Urodyn* 2011;**30**:1300–4.
25. Tong YC. Comparisons of urodynamic findings and voiding habits in patients with concomitant benign prostatic hyperplasia and detrusor overactivity presenting with or without the symptom of urgency. *Urol Int* 2007;**78**:219–25.
26. Rapp DE, Neil NJ, Govier FE, Kobashi KC. Bladder sensation measures and overactive bladder. *J Urol* 2009;**182**:1050–4.
27. Tsunoyama K, Sakakibara R, Yamaguchi C, Uchiyama T, Yamamoto T, Yamanishi T, et al. Pathogenesis of reduced or increased bladder sensation. *Neurourol Urodyn* 2011;**30**:339–43.
28. Barry MJ, Fowler Jr FJ, O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK. Correlation of the American Urological Association symptom index with self-administered versions of the Madsen-Iversen, Boyarsky and Maine Medical Assessment Program symptom indexes. Measurement Committee of the American Urological Association. *J Urol* 1992;**148**:1558–63.
29. Cockett A, Aso Y, Denis L, et al. Recommendation of the International Consensus Committee concerning: 1. Prostate symptom score and quality of life assessment. In: Cockett ATK, Khoury S, Aso Y, et al., editors. *Proceedings, The 2nd International Consultation on Benign Prostatic Hyperplasia (BPH), Paris, June 27-30, 1993*. Jersey, Channel Islands: Scientific Communication International Ltd; 1994. p. 553–5.
30. Hartmann KE, McPheeters ML, Biller DH, Ward RM, McKoy JN, Jerome RN, et al. *Treatment of Overactive Bladder in Women (Evidence Report/Technology Assessment Number 187 (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2007-10065-I))*. Agency for Healthcare Research and Quality (AHRQ); 2009.
31. Panayi DC, Tekkis P, Fernando R, Hendricken C, Khullar V. Ultrasound measurement of bladder wall thickness is associated with the overactive bladder syndrome. *Neurourol Urodyn* 2010;**29**:1295–8.
32. Cumpanas AA, Botoca M, Minciu R, Bucuras V. Intravesical prostatic protrusion can be a predicting factor for the treatment outcome in patients with lower urinary tract symptoms due to benign prostatic obstruction treated with tamsulosin. *Urology* 2013;**81**:859–63.
33. Fitzgerald MP, Brubaker L. Variability of 24-hour voiding diary variables among asymptomatic women. *J Urol* 2003;**169**:207–9.
34. Homma Y, Yoshida M, Seki N, Yokoyama O, Kakizaki H, Gotoh M, et al. Symptom assessment tool for overactive bladder syndrome–overactive bladder symptom score. *Urology* 2006;**68**:318–23.
35. Blaivas JG, Panagopoulos G, Weiss JP, Somaroo C. Validation of the overactive bladder symptom score. *J Urol* 2007;**178**:543–7.
36. Reese PR, Pleil AM, Okano GJ, Kelleher CJ. Multinational study of reliability and validity of the King's Health Questionnaire in patients with overactive bladder. *Qual Life Res* 2003;**12**:427–42.
37. Kelleher CJ, Cardozo LD, Khullar V, Salvatore S. A new questionnaire to assess the quality of line of urinary incontinent women. *Br J Obstet Gynaecol* 1997;**104**:1374–9.
38. Michel MC, Oelke M, Vogel M, de la Rosette JJ. Which single-item measures of overactive bladder symptom treatment correlate best with patient satisfaction? *Neurourol Urodyn* 2011;**30**:510–4.
39. Hung MJ, Chou CL, Yen TW, Chuang YC, Meng E, Huang ST, et al. Development and validation of the Chinese Overactive Bladder Symptom Score for assessing overactive bladder syndrome in a RESORT study. *J Formos Med Assoc* 2013;**112**:276–82.
40. Liao CH, Chung SD, Kuo HC. Diagnostic value of International Prostate Symptom Score voiding-to-storage subscore ratio in male lower urinary tract symptoms. *Int J Clin Pract* 2011;**65**:552–8.
41. Liao CH, Lin VC, Chung SD, Kuo HC. Therapeutic effect of α-blockers and antimuscarinics in male lower urinary tract symptoms based on the International Prostate Symptom Score subscore ratio. *Int J Clin Pract* 2012;**66**:139–45.
42. Jiang YH, Lin VC, Liao CH, Kuo HC. International Prostatic Symptom Score-voiding/storage subscore ratio in association with total prostatic volume and maximum flow rate is diagnostic of bladder outlet-related lower urinary tract dysfunction in men with lower urinary tract symptoms. *PLoS One* 2013;**8**:e59176.
43. Tibaek S, Gard G, Klarskov P, Iversen HK, Dehlendorff C, Jensen R. Prevalence of lower urinary tract symptoms (LUTS) in stroke patients: a cross-sectional, clinical survey. *Neurourol Urodyn* 2008;**27**:763–71.
44. Kovindha A, Wattanapan P, Dejpratham P, Permsirivanich W, Kuptniratsaikul V. Prevalence of incontinence in patients after stroke during rehabilitation: a multi-centre study. *J Rehabil Med* 2009;**41**:489–91.
45. Singhania P, Andankar MG, Pathak HR. Urodynamic evaluation of urinary disturbances following traumatic brain injury. *Urol Int* 2010;**84**:89–93.
46. Ragab MM, Mohammed ES. Idiopathic Parkinson's disease patients at the urologic clinic. *Neurourol Urodyn* 2011;**30**:1258–61.
47. Ransmayr GN, Holliger S, Schletterer K, Heidler H, Deibl M, Poewe W, et al. Lower urinary tract symptoms in dementia with Lewy bodies, Parkinson disease, and Alzheimer disease. *Neurology* 2008;**70**:299–303.
48. Liu RT, Chung MS, Lee WC, Chang SW, Huang ST, Yang KD, et al. Prevalence of overactive bladder and associated risk factors in 1359 patients with type 2 diabetes. *Urology* 2011;**78**:1040–5.
49. Bansal R, Agarwal MM, Modi M, Mandal AK, Singh SK. Urodynamic profile of diabetic patients with lower urinary tract symptoms: association of diabetic cystopathy with autonomic and peripheral neuropathy. *Urology* 2011;**77**:699–705.
50. Dib PT, Trigo-Rocha F, Gomes CM, Srougi M. Urodynamic evaluation in diabetic patients with prostate enlargement and lower urinary tract symptoms. *Urol Int* 2008;**80**:378–82.
51. Lee SH, Chung BH, Kim SJ, Kim JH, Kim JC, Lee JY. Initial combined treatment with anticholinergics and α-blockers for men with lower urinary tract symptoms related to BPH and overactive bladder: a prospective, randomized, multi-center, double-blind, placebo-controlled study. *Prostate Cancer Prostatic Dis* 2011;**14**:320–5.
52. Toh KL, Ng CK. Urodynamic studies in the evaluation of young men presenting with lower urinary tract symptoms. *Int J Urol* 2006;**13**:520–3.
53. Kuo HC. Videourodynamic analysis of pathophysiology of men with both storage and voiding lower urinary tract symptoms. *Urology* 2007;**70**:272–6.
54. Gomes CM, Nunes RV, Araújo RM, Sacomani CR, Trigo-Rocha FE, Bruschini H, et al. Urodynamic evaluation of patients with lower urinary tract symptoms and small prostate volume. *Urol Int* 2008;**81**:129–34.
55. Reynard JM, Abrams P. Bladder-outlet obstruction–assessment of symptoms. *World J Urol* 1995;**13**:3–8.
56. Reynard JM, Yang Q, Donovan JL, Peters TJ, Schafer W, de la Rosette JJ, et al. The ICS-'BPH'Study: uroflowmetry, lower urinary tract symptoms and bladder outlet obstruction. *Br J Urol* 1998;**82**:619–23.
57. Abrams P, Schafer W, Tammela TL, Barrett DM, Hedlund H, Rollema HJ, et al. Improvement of pressure flow parameters with finasteride is greater in men with large prostates. Finasteride Urodynamics Study Group. *J Urol* 1999;**161**:1513–7.
58. Al-Zahrani AA, Gajewski JB. Association of symptoms with urodynamic findings in men with overactive bladder syndrome. *BJU Int* 2012;**110**:E891–5.
59. de la Rossette JJ, Witjes WP, Schafer W, Abrams P, Donovan JL, Peters TJ, et al. Relationships between lower urinary tract symptoms and bladder outlet obstruction: results from the ICS-"BPH" study. *Neurourol Urodyn* 1998;**17**:99–108.
60. Witjes WP, Aanink RG, Ezz-el-Din K, Wijkstra H, Debruyne EM, de la Rosette JJ. The correlation between prostate volume, transition zone volume, transition zone index and clinical and urodynamic investigations in patients with lower urinary tract symptoms. *Br J Urol* 1997;**80**:84–90.
61. Kuo HC. Pathophysiology of lower urinary tract symptoms in aged men without bladder outlet obstruction. *Urol Int* 2000;**64**:86–92.
62. Oelke M, Baard J, Wijkstra H, de la Rosette JJ, Jonas U, Höfner K, et al. Age and bladder outlet obstruction are independently associated with detrusor overactivity in patients with benign prostatic hyperplasia. *Eur Urol* 2008;**54**:419–26.
63. Romanzi LJ, Groutz A, Heritz DM, Blaivas JG. Involuntary detrusor contractions: correlation of urodynamic data to clinical categories. *Neurourol Urodyn* 2001;**20**:249–57.
64. Digesu GA, Khullar V, Cardozo L, Salvatore S. Overactive bladder syndrome: Do we need urodynamics? *Neurourol Urodyn* 2003;**22**:105–8.
65. Laniado ME, Ockrim JL, Marronaro A, Tubaro A, Carter SS. Serum prostate-specific antigen to predict the presence of bladder outlet obstruction in men with urinary symptoms. *BJU Int* 2004;**94**:1283–6.
66. Eckhardt MD, van Venrooij GE, Boon TA. Symptoms, prostate volume, and urodynamic findings in elderly male volunteers without and with LUTS and in patients with LUTS suggestive of benign prostatic hyperplasia. *Urology* 2001;**58**:966–71.
67. Flisser AJ, Blaivas JG. Role of cystometry in evaluating patients with overactive bladder. *Urology* 2002;**60**:33–42.
68. Hyman MJ, Groutz A, Blaivas JG. Detrusor instability in men: Correlation of lower urinary tract symptoms with urodynamic findings. *J Urol* 2001;**166**:550–3.
69. Hashim H, Abrams P. Is the bladder a reliable witness for predicting detrusor overactivity? *J Urol* 2006;**175**:191–5.
70. Vecchioli-Scaldazza C, Grinta R. Overactive bladder syndrome: what is the role of evidence of detrusor overactivity in the cystometric study? *Minerva Urol Nefrol* 2010;**62**:355–61.

71. Malone-Lee JG, Al-Buheissi S. Does urodynamic verification of overactive bladder determine treatment success? Results from a randomized placebo-controlled study. *BJU Int* 2009;**103**:931–7.
72. Rovner E, Kennelly M, Schulte-Baukloh H, Haag-Molkenteller C, Dasgupta P. Urodynamic results and clinical outcomes with intradetrusor injections of onabotulinumtoxinA in a randomized, placebo-controlled dose-finding study in idiopathic overactive bladder. *Neurourol Urodyn* 2011;**30**:556–62.
73. Thüroff JW, Abrams P, Andersson KE, Artibani W, Chapple CR, Drake MJ, et al. EAU Guidelines on Urinary Incontinence. *Actas Urol Esp* 2011;**35**:373–88.
74. Chapple CR. Muscarinic receptor antagonist in the treatment of overactive bladder. *Urology* 2000;**55**:33–46.
75. Jarvis GJ. A controlled trial of bladder drill and drug therapy in the management of detrusor instability. *Br J Urol* 1981;**53**:565–6.
76. Burgio KL, Goode PS, Johnson TM, et al. Behavioral versus drug treatment for overactive bladder in men: the Male Overactive Bladder Treatment in Veterans (MOTIVE) trial. *J Am Geriatr Soc* 2011;**59**:2209–16.
77. Fantl JA, Wyman JF, McClish DK, Harkins SW, Elswick RK, Taylor JR, et al. Efficacy of bladder training in older women with urinary incontinence. *JAMA* 1991;**265**:609–13.
78. Hashim H, Abrams P. How should patients with an overactive bladder manipulate their fluid intake? *BJU Int* 2008;**102**:62–6.
79. Bryant CM, Dowell CJ, Fairbrother G. Caffeine reduction education to improve urinary symptoms. *Br J Nurs* 2002;**11**:560–5.
80. Kaya S, Akbayrak T, Beksac S. Comparison of different treatment protocols in the treatment of idiopathic detrusor overactivity: a randomized controlled trial. *Clin Rehabil* 2011;**25**:327–38.
81. Subak LL, Wing R, West DS, Franklin F, Vittinghoff E, Creasman JM, et al. Weight loss to treat urinary incontinence in overweight and obese women. *NEJM* 2009;**360**:481–90.
82. Kafri R, Langer R, Dvir Z, Katz-Leurer M. Rehabilitation vs drug therapy for urge urinary incontinence: short-term outcome. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;**18**:407–11.
83. Ouslander JG. Management of overactive bladder. *N Eng J Med* 2004;**350**:786–99.
84. Yarker Y, Goa KL, Fitton A. Oxybutynin A review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic use in detrusor instability. *Drugs Aging* 1995;**6**:243–62.
85. Andersson KE. LUTS treatment: future treatment options. *Neurourol Urodyn* 2007;**26**:934–47.
86. Athanasopoulos A, Gyftopoulos K, Giannitsas K, Fisfis J, Perimenis P, Barbalias G. Combination treatment with an alpha-blocker plus an anticholinergic for bladder outlet obstruction: a prospective, randomized, controlled study. *J Urol* 2003;**169**:2253–6.
87. Athanasopoulos A, Chapple C, Fowler C, Gratzke C, Kaplan S, Stief C, et al. The role of antimuscarinics in the management of men with symptoms of overactive bladder associated with concomitant bladder outlet obstruction: an update. *Eur Urol* 2011;**60**:94–105.
88. Liao CH, Kuo YC, Kuo HC. Predictors of successful first-line antimuscarinic monotherapy in men with enlarged prostate and predominant storage symptoms. *Urology* 2013;**81**:1030–3.
89. Ohlstein EH, von Keitz A, Michel MC. A multicenter, double-blind, randomized, placebo-controlled trial of the β3-adrenoceptor agonist solabegron for overactive bladder. *Eur Urol* 2012;**62**:834–40.
90. Scheife R, Takeda M. Central nervous system safety of anticholinergic drugs for the treatment of overactive bladder in the elderly. *Clin Ther* 2005;**27**:144–53.
91. Chung SD, Chang HC, Chiu B, Liao CH, Kuo HC. The efficacy of additive tolterodine extended release for 1-year in older men with storage symptoms and clinical benign proastatic hyperplasia. *Neurourol Urodyn* 2011;**30**:568–71.
92. Yamaguchi O, Kakizaki H, Homma Y, Takeda M, Nishizawa O, Gotoh M, et al. Solifenacin as add-on therapy for overactive bladder symptoms in men treated for lower urinary tract symptoms–ASSIST, randomized controlled study. *Urology* 2011;**78**:126–33.
93. Kaplan SA, Roehrborn CG, Gong J, Sun F, Guan Z. Add-on fesoterodine for residual storage symptoms suggestive of overactive bladder in men receiving α-blocker treatment for lower urinary tract symptoms. *BJU Int* 2012;**109**:1831–40.
94. Kaplan SA, McCammon K, Fincher R, Fakhoury A, He W. Safety and tolerability of solifenacin add-on therapy to α-blocker treated men with residual urgency and frequency. *J Urol* 2013;**189**:S129–34.
95. Chapple C, Sievert KD, MacDiarmid S, Khullar V, Radziszewski P, Nardo C, et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. *Eur Urol* 2013;**64**:249–56.
96. Mohee A, Khan A, Harris N, Eardley I. Long-term outcome of the use of intravesical botulinum toxin for the treatment of overactive bladder (OAB). *BJU Int* 2013;**111**:106–13.
97. Fowler CJ, Auerbach S, Ginsberg D, Hale D, Radziszewski P, Rechberger T, et al. OnabotulinumtoxinA improves health-related quality of life in patients with urinary incontinence due to idiopathic overactive bladder: a 36-week, double-blind, placebo-controlled, randomized, dose-ranging trial. *Eur Urol* 2012;**62**:148–57.
98. Kuo HC. Reduction of urgency severity is associated with long-term therapeutic effect after intravesical onabotulinumtoxin A injection for idiopathic detrusor overactivity. *Neurourol Urodyn* 2011;**30**:1497–502.
99. Liao CH, Kuo HC. Increased risk of large post-void residual urine and decreased long-term success rate after intravesical onabotulinumtoxinA injection for refractory idiopathic detrusor overactivity. *J Urol* 2013;**189**:1804–10.
100. Dowson C, Watkins J, Khan MS, Dasgupta P, Sahai A. Repeated botulinum toxin type A injections for refractory overactive bladder: medium-term outcomes, safety profile, and discontinuation rates. *Eur Urol* 2012;**61**:834–9.
101. Kuo HC, Liao CH, Chung SD. Adverse events of intravesical botulinum toxin a injections for idiopathic detrusor overactivity: risk factors and influence on treatment outcome. *Eur Urol* 2010;**58**:919–26.
102. de Sèze M, Raibaut P, Gallien P, Even-Schneider A, Denys P, Bonniaud V, et al. Transcutaneous posterior tibial nerve stimulation for treatment of the overactive bladder syndrome in multiple sclerosis: results of a multicenter prospective study. *Neurourol Urodyn* 2011;**30**:306–11.
103. Peters KM, MacDiarmid SA, Wooldridge LS, Leong FC, Shobeiri SA, Rovner ES, et al. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. *J Urol* 2009;**182**:1055–61.
104. MacDiarmid SA, Peters KM, Shobeiri SA, Wooldridge LS, Rovner ES, Leong FC, et al. Long-term durability of percutaneous tibial nerve stimulation for the treatment of overactive bladder. *J Urol* 2010;**183**:234–40.
105. Leng WW, Chancellor MB. How sacral nerve stimulation neuromodulation works. *Urol Clin North Am* 2005;**32**:11–8.
106. Hassouna MM, Siegel SW, Nyeholt AA, Elhilali MM, van Kerrebroeck PE, Das AK, et al. Sacral neuromodulation in the treatment of urgency-frequency symptoms: A multicenter study on efficacy and safety. *J Urol* 2000;**163**:1849–54.
107. Sutherland SE, Lavers A, Carlson A, Holtz C, Kesha J, Siegel SW. Sacral nerve stimulation for voiding dysfunction: One institution's 11-year experience. *Neurourol Urodyn* 2007;**26**:19–28.
108. van der Pal F, Heesakkers JP, Bemelmans BL. Current opinion on the working mechanisms of neuromodulation in the treatment of lower urinary tract dysfunction. *Curr Opin Urol* 2006;**16**:261–7.
109. Sriplakich S, Promwatcharanon K. The resolution of detrusor over activity after medical and surgical treatment in patients with bladder outlet obstruction. *J Med Assoc Thai* 2007;**90**:2326–31.
110. Seki N, Yuki K, Takei M, Yamaguchi A, Naito S. Analysis of the prognostic factors for overactive bladder symptoms following surgical treatment in patients with benign prostatic obstruction. *Neurourol Urodyn* 2009;**28**:197–201.
111. Appell RA. Surgery for the treatment of overactive bladder. *Urology* 1998;**51**:27–9.
112. Kuo HC. Clinical outcome and quality of life after enterocystolplasty for contracted bladders. *Urol Int* 1997;**58**:160–5.
113. Lotenfoe RR, Christie J, Parsons A, Burkett P, Helal M, Lockhart JL. Absence of neuropathic pelvic pain and favorable psychological profile in the surgical selection of patients with disabling interstitial cystitis. *J Urol* 1995;**154**:2039–42.